In vitro reprogramming of mouse and human somatic cells to an embryonic state

Grant Award Details

In vitro reprogramming of mouse and human somatic cells to an embryonic state

Grant Type: New Faculty I

Grant Number: RN1-00564

Project Objective: The overall objective of this grant was to investigate the molecular mechanisms underlying reprogramming of mouse and human somatic cells to pluripotency.

Investigator:

Name: Kathrin Plath

Institution: University of California, Los Angeles

Type: PI

Disease Focus: Neurological Disorders, Rett's Syndrome

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $2,229,427

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Grant Application Details

Application Title: In vitro reprogramming of mouse and human somatic cells to an embryonic state

Public Abstract:

Embryonic stem (ES) cells are remarkable cells in that they can replicate themselves indefinitely and have the potential to turn into all possible cell type of the body under appropriate environmental conditions. These characteristics make ES cells a unique tool to study development in the culture dish and put them at center stage for regenerative medicine. Two techniques, one called somatic cell nuclear transfer (SCNT) and the other in vitro reprogramming, have shown that adult cells from the mouse can be reverted to an ES like state. In SCNT, adult cell nuclei are transferred into oocytes and allowed to develop as early embryos from which ES cells can be derived, while in the in vitro method four genes are ectopically activated in the adult cell nucleus to induce an embryonic state in the culture dish. Key requirement for both processes is to erase the memory of the adult cell that specifies it as an adult cell and set up the ES cell program. How this happens remains unclear, and if it can be reproduced with human adult cells is an open question. Therefore, we will attempt to use the in vitro reprogramming method to generate human ES cells from adult cells and begin to understand the mechanism of the reprogramming process in both human and mouse cells. In addition to being integral to improving our understanding of how ES cells develop, if successful, this work will provide an important milestone for regenerative medicine. Many debilitating diseases and conditions are caused by damage to cells and tissue. In vitro reprogramming could provide a way to generate patient-specific stem cells that, in culture, could be turned into the type of cell or tissue needed to cure the patient's disease or injury and transplanted back into the patient's body. For example, Parkinson's disease is caused by the loss or destruction of nerve cells. If reprogramming becomes possible, we could take a skin biopsy from a patient with Parkinson's disease, induce the embryonic state in those skin cells to then be able to turn them into nerve cells and transplant them back into the same donor patient. Reprogramming could also be used to repair spinal cord injuries, allowing people who are paralyzed by accidents to walk again, or be helpful for patients with juvenile diabetes. One important advantage of patient-specific self-transplants is that they obviate the need for immunosuppression, which is often problematic for the patient. In addition, human cell reprogramming could be a new way to study how diseases progress at the cellular level as reprogramming could generate ES cells from patients with complex diseases that can be studied in detail for what makes them go awry during development. This knowledge could speed the search for new treatments and possibly cures for some of the most complex diseases that affect societies. We hope that the knowledge gained from our studies on reprogramming can, someday, support research that will help to put these idea to clinical use.

Statement of Benefit to California:	Donated organs and tissues are often used to replace those that are diseased or destroyed, but unfortunately, the number of people needing a transplant exceeds the number of organs available for transplantation. Embryonic stem (ES) cells can be propagated in the laboratory for an unlimited period of time and can turn into all the specialized cell types that make us a human being. Therefore, ES cells offer the possibility of a renewable source of replacement cells and tissues to treat diseases, conditions, and disabilities such as Parkinson's and Alzheimer's, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis and rheumatoid arthritis. Our research is aimed to generate ES cells from adult cells through a method called in vitro reprogramming and to understand the mechanism by which the ES cell program can be reinstated in the adult cells. This work will not only provide the foundation for a better understanding of how human ES cells develop, but, if successful, be an important milestone for regenerative medicine. The advantage of using ES cells derived from adult cells by in vitro reprogramming would be that the patient's own cells could be reprogrammed to an ES cell state and therefore, when transplanted back into the patient, not be attacked and destroyed by the body's immune system. This would be beneficial to the people of California as tens of millions of Americans suffer from diseases and injuries that could benefit from research of in vitro reprogramming. Such advances would benefit the health as well as the economy of the state of California.